Audit of blood product transfusion in paediatric congenital heart surgery on cardiopulmonary bypass

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Declaration

I, Caroline Tumelo Bayebaye, herewith declare that this research report is my own, unaided work. It is being submitted for the degree of Master of Medicine at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other University.

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Candidate's signature

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Date

I dedicate this work to my family and friends who have supported me emotionally during this journey. I thank my colleagues for helping me with the grammar in this research project. It was not easy, but now I have completed the work.

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List of abbreviations

ABD	autologous blood transfusion
AOX	aortic cross-clamp
Antif	antifibrinolytic
ASD	atrial septal defect
AVSD	atrio-ventricular septal defect
CPB	cardiopulmonary bypass
CS	cell saver
FFP	fresh frozen plasma
Hct	haematocrit
Hb	haemoglobin
ICU	intensive care unit
MUF	modified ultrafiltration
RACHS	risk adjusted classification for congenital heart surgery
RPC	red packed cells
SANBS	South African National Blood Services
TAPVD	total anomalous pulmonary venous disease
TGV	transposition of great vessels
TOF	tetralogy of Fallot
TXA	tranexamic acid
VSD	ventricular septal defect
WHO	World Health Organisation

Abstract

Background

Cardiac surgery is associated with perioperative bleeding which may result in the need for blood transfusion, particularly in paediatric congenital cardiac surgery performed on cardiopulmonary bypass (CPB). Regular auditing of practices is imperative for improvements to be realised.

Methods

Retrospective, contextual, descriptive data of 105 patients were collected for the period January to December 2014.

Results

The median age of patients was 4 (1–6) years, weight 13 (8.4–20) kg, with mean lowest CPB haemoglobin of 8.3 (1.5) g/dL. There was a statistically significant difference in median red packed cells (RPC), platelet and cryoprecipitate units transfused per patient across Risk Adjusted classification for Congenital Heart Surgery categories ($p=0.03$, $p=0.0013$, $p=0.0001$). There was a statistically significant correlation between transfused fresh frozen plasma units with CPB time ($r=0.2634$, $p=0.0199$) and RPC units transfused ($r=-0.4654$, $p<0.001$).

Conclusion

Although no standardised transfusion guidelines were available, overall blood product transfusion was comparable to previous reports.

SECTION 1

Literature Review

1.1 Introduction

This literature review will start with a brief history of blood transfusion, and cardiac surgery in paediatric patients. A discussion of the different blood products, and factors contributing to the transfusion of blood products during paediatric cardiac surgery will be discussed. The complications related to blood product transfusion, and the guidelines to transfuse blood products during paediatric cardiac surgery will be explored. A discussion on blood conservation strategies, the benefits of the implementation of these strategies, and the cost implications of blood product transfusion will also be discussed. A review of practices by other institutions with regards to utilisation of blood products will be reviewed.

1.2 Brief history of blood transfusion and paediatric cardiac surgery

The history of blood transfusion goes as far back as the discovery of the circulatory system in 1616. Blood transfusion evolved from drinking of blood by Pope Innocent VIII, although not considered a true transfusion, to transfusion of a dog by Richard Lower, in 1665. This was followed by the first transfusion of man by Denis in 1667, and the discovery of an incompatibility reaction. Carl Landsteiner, in 1900, described the existence of three blood groups. The first blood bank was subsequently established in 1934 at the Cook Country Hospital, in Chicago. (1)

The first paediatric cardiac operation was performed by Clarence Crafoord in Sweden. He repaired a coarctation of the aorta in a 12 year old boy on 19 October 1944 (2), this was before development of the cardiopulmonary (CPB) machine where. Russell M. Nelson performed the first successful paediatric cardiac operation on CPB at the Salt Lake General Hospital in March 1956. He performed a total repair of tetralogy of Fallot on a four year old girl (3).

The evolution and development of blood products and CPB machines has made it possible for surgeons to operate on complex cardiac conditions with great success.

1.3 Blood products

The use of blood products has become common practice for health care workers. Red packed cells (RPC), platelets, fresh frozen plasma (FFP), and cryoprecipitate are the commonly used blood products in paediatric cardiac surgery, and will be briefly discussed.

1.3.1 Red packed cells

RPC are concentrated red blood cells collected after removal of plasma, platelets, and leucocytes (buffy layer) from whole blood. The concentrated red blood cells collected have a haematocrit (Hct) level of 70 to 80% which is reduced to a Hct of 55% by the addition of normal saline and preservatives. The added preservatives include adenine for generation of ATP, glucose for energy, citrate to prevent clotting, saline, and mannitol to maintain cell integrity during the storage period. RPC can be stored for 42 days at 1 to 6 °C (4, 5). The recommended dosing for RPC in paediatric patients less than four months is 10 to 20 ml/kg, and above four months it is calculated according to the equation:

Dose (mL)= desired haemoglobin (Hb) rise (g/dL) x weight (kg) x3. (6)

The use of leucocyte depleted RPC is recommended in children less than one year of age (6). Leucocytes have been implicated in immunomodulation, transmission of cytomegalovirus (6), and the initiation of an inflammatory response which is worsened by the use of CPB (7).

1.3.2 Platelets

Platelets are fragments of cytoplasm formed from megakaryocytes and have a biconvex discoid shape with a diameter of 2 to 3 µm (4). They are used to prevent or treat bleeding disorders that might be due to thrombocytopenia or decreased function of platelets (5).

Platelets are collected by the centrifugation of whole blood within eight hours of collection, and are then kept viable by continuous agitation to ensure oxygenation and prevent clumping. They are stored at room temperature for five days as this is their life span outside the body (4, 5). The transfusion dose of platelets is 5-10 ml/kg in neonates and 10 to 20 ml/kg in infants (6).

1.3.3 Fresh frozen plasma

FFP is plasma collected from whole blood by centrifugation and separation, then frozen within eight hours of collection and stored at -18 °C. The plasma consists of

normal volume of all clotting proteins, albumin, immunoglobulins, and 70% of plasma factor VIII as a dilute solution of 200 to 250 ml. The FFP must be thawed before usage at 36 °C to defrost (4, 5). It is usually infused when there is coagulation factor deficiency, to reverse anticoagulation, and during massive bleeding at a dose of 10-15 ml/kg (8).

1.3.4 Cryoprecipitate

Cryoprecipitate is a precipitate of thawed plasma consisting of concentrated clotting proteins. The clotting proteins are fibrinogen, fibronectin, von Willebrand factor, factor V, factor VIII, and factor XIII in a volume of 15-20 ml (4, 9). It is transfused during massive transfusion, or when there is fibrinogen deficiency. The recommended transfusion dose is 5 ml/kg for neonates (6), and one unit per 5-10 kg for infants and children (8).

1.4 Factors that influence blood products transfusion in paediatric cardiac surgery

Indications for transfusion of blood products in the paediatric cardiac patient are multifactorial. Factors that will be discussed are type of congenital cardiac condition, age, weight of the patient and CPB related factors.

1.4.1 Congenital cardiac conditions

Corrective surgery for congenital cardiac conditions is categorised by the Risk Adjusted classification for Congenital Heart Surgery (RACHS) scoring system. Each category signifies the complexity of the operation as the category number increases, and is associated with increasing risk of bleeding (10).

Congenital cardiac conditions are associated with activation of the coagulation cascade secondary to shear stress from turbulent flow of blood (11), resulting in a decrease in platelet count and consumption of clotting factors (12). These abnormalities are more pronounced in cyanotic cardiac conditions, hence the focus on studying other mechanisms causing coagulopathy (12).

Patients with cyanotic cardiac conditions are at an increased risk of bleeding because of the acquired haemostatic disorder (13) as a result of chronic hypoxaemia. The chronic hypoxaemia and hypoxia stimulates the release of erythropoietin by the kidneys, resulting in erythrocytosis (11). This secondary erythrocytosis leads to blood hyperviscosity which causes shear stress activating platelets and resulting in thrombocytopenia and an increase in number of micro particles (14, 15). The

secondary erythrocytosis has also been implicated in causing fibrinogen dysfunction (16). These abnormalities could be the reason for the increased risk in postoperative bleeding in cyanotic infants when compared to the acyanotic patients (17).

Other causes of thrombocytopenia in cyanotic patients is underproduction of platelets as a result of erythrocytosis in the fixed intravascular volume (13), and failure of fragmentation of megakaryocytes as they bypass the lungs (15). There is an associated decrease in cardiac output, liver congestion and liver dysfunction as a result of hypoxaemia. The liver dysfunction causes a decrease in liver production of clotting factors, especially vitamin K dependent factors (factor II, V, VII, IX, X) contributing to the coagulopathy (11).

1.4.2 Age and weight of child

Neonates have an immature hepatic system resulting in reduced function of clotting factor production predisposing them to bleeding. Adult levels of clotting factors are only reached between 6 to 12 months of age (18). Neonates might have a normal platelet count, but their function is decreased until 2 to 4 weeks after birth (19). This becomes a problem when the patient is younger than 12 months, and has to be on CPB, as CPB is associated with coagulopathy secondary to haemodilution (18, 20).

Kipps et al (21) conducted a study demonstrating that young age, lower weight at surgery, and prematurity are associated with increased risk for blood product transfusion.

1.4.3 Cardiopulmonary bypass

CPB is a none physiological system (18) that is used to temporarily take over the function of the heart and lungs during open cardiac surgery. Heparin must be given to the patient before initiation of the CPB machine to prevent thrombosis. This thrombosis is caused by blood contact with the CPB circuit resulting in contact activation of thrombin and clotting factors, which initiates the coagulation cascade. This results in consumption of clotting factors predisposing to bleeding (22).

CPB is associated with impairment of haemostasis due to the dilution of the patients (Hb), clotting factors (18), platelet, and fibrinogen levels (17). The dilution is exaggerated in the paediatric population due to their small total blood volume relative to the CPB machine, hence the use of FFP prime in neonates (17). Priming the CPB circuit with RPC is perfomed to obtain the desired Hb on CPB (23).

In order to attenuate the haemodilution caused by CPB circuit prime, priming with RPC and FFP is commonly practiced in paediatric congenital cardiac surgery on CPB (24-26). However, studies conducted to compare priming with colloid to FFP, found no difference in risk of bleeding between the groups (13, 27, 28). A study in neonates and infants, in contrast, demonstrated reduced bleeding in patients with FFP when compared to albumin prime, due to preservation of fibrinogen level (29).

The risk of transfusion of blood products is increased in complex and emergency operations, and in very young patients with a low preoperative red blood cell volume (9, 30). The risk is also increased by prolonged aortic cross clamp and CPB time (21, 31, 32) .

1.5 Complications of blood product transfusion

Transfusion of blood products is a common practice in the hospital and it is important to know its complications in order to obtain informed patient consent and detect adverse effects early if they arise. The South African National Blood Service (SANBS) has adopted a haemovigilance programme since 2001. This programme consists of processes intended to improve quality, and safety of transfused blood products by using appropriate screening tests, and monitoring the blood transfusion chain from donor to recipient. The monitoring process includes risk management, reporting of adverse transfusion reactions, and auditing blood product usage to see whether blood products are transfused following guidelines or wasted (33, 34). Complications associated with transfusion of blood products are discussed below.

1.5.1 General complications of blood transfusion

The most common complication of transfusion of blood products is due to human errors, which are as high as 77% according to the 2016 Serious Hazards of Transfusion Report (35). These errors are preventable by taking precautions during blood specimen handling. It requires the collection of the blood specimen into an appropriate tube which is correctly labelled, and proper handling by the blood bank personnel. The health care workers should also recheck the patient's details with the issued unit before the transfusion of the blood product unit is initiated. The infectious and non-infectious complications as well as the CBP related complications are shown in Table 1.1.

1.5.2 Infectious

In South Africa, the incidence of transfusion transmitted infection is minimal (Table 1.1) from the statistics by the SANBS 2007. The reason for the low incidence for transfusion transmitted infections might be because of the introduction of nucleic acid amplification testing, since 2005, by SANBS, and failure to follow and report cases by health care workers (36). The risk of infection increases with the amount of products transfused during the operation (21), this could also be due to immunomodulation ensuing in immunosuppression.

Table 1.1 SANBS reported incidence of infection and infectious agents (34)

Infectious agent	**Period**	**Incidence**
Virus		
HIV	2001 to 2007	6 cases reported
Hepatitis B	2005 to 2007	Donor prevalence of 0.077
Hepatitis C	2005 to 2007	Donor prevalence of 0.0062
Bacteria		
RPC	2000 to 2007	7 cases
Platelets Apheresis	2007	7/530 cases tested positive
Parasites		
Malaria	2007	No cases reported

1.5.3 Non-infectious

Non-infectious blood product transfusion complications are problematic because they are not preventable. These complications are solely dependent on the patient's immune system response.

The haemolytic transfusion reaction is preceded by antibody-antigen incompatibility in plasma during the transfusion of blood products. This complication can occur within minutes to 24 hours (early), or 2 to 21 days (delayed) post transfusion of blood products. The early reaction occurs due to ABO incompatibility or alloantibodies causing intravascular haemolysis and the destruction of transfused or recipient blood. The delayed reaction is caused by incompatibility of rare blood groups, for example Rhesus and Kidd, resulting in extravascular haemolysis (5). The allo-immunisation

caused by transfusion of blood products can result in acute lung injury, haemolytic reactions, transplant rejection, and allo-immune thrombocytopenia (37).

The non-haemolytic reaction is due to sensitisation of the patient's immune system to donated white cells, platelets or plasma proteins (5). The manifestations ranges from a simple allergic reaction mediated by immunoglobulin E to an anaphylactic reaction commonly seen in immunoglobulin A deficient patients when blood products having anti-immunoglobulin A antibodies are transfused (38).

The most complex non-haemolytic reaction is post transfusion purpura which is caused by developed platelet alloantibodies attacking the patient's platelets resulting in thrombocytopenia (5).

Graft versus host disease is a rare and delayed transfusion reaction caused by donor lymphocytic cells mounting an immune response against the immunocompromised host tissue (38).

Massive transfusion in paediatric patients is defined as a transfusion of greater than 40 ml/kg (39) or replacement of the patient's blood volume within six hours (6). Ranucci et al (40) states that the small paediatric patient is prone to massive transfusion due to their small blood volumes. The sole transfusion of RPC causes consumption of platelets and clotting factors which results in dilution coagulopathy leading to disseminated intravascular coagulopathy. This coagulopathy is worsened by hypothermia caused by infusing cold blood products resulting in an unfavourable environment for normal functioning of clotting enzymes (38).

Massive RPC transfusion can result in citrate toxicity causing hypocalcaemia, and hypomagnesaemia due to chelation with citrate which produces myocardial suppression and coagulopathy. The metabolic derangement caused by citrate (38) can result in electrolyte abnormalities (8) further compromising cardiovascular function.

Stored RPCs are at different stages of aging. Aged blood has a decrease in 2,3 diphosphoglycerate resulting in a left shift of the oxygen dissociation curve causing poor oxygenation of tissues, and is also associated with renal and pulmonary morbidities (40). There is hyperkalaemia caused by potassium leak from stored RPC due to none functional Na^+-K^+ ATPase pump from ATP deficiency (38).

1.5.4 Cardiopulmonary bypass related complications

The inflammatory response in paediatric cardiac surgery on CPB is multifactorial. It is caused by the stress response to cardiac surgery, contact of patient blood with the CPB circuit, and transfusion of blood products. The response may result in multiple organ dysfunction depending on the severity (41).

Cardiac surgery results in an inflammatory response due to the body's humoral and cellular response to injury (42, 43). Contact of blood with the CPB circuit causes cytokine production and activation of neutrophils, platelets and the complement system (22). This response is worse in children because their small blood volume is exposed to a relatively large CPB circuit surface (41, 44).

Another source of this inflammatory response occurs after releasing of the aortic cross clamp; the reperfusion of previously ischaemic tissues discharges endotoxins and cytokine systematically (42). This results in endothelial activation, evidenced by release of intracellular lysosomes' granular contents and the generation of oxygen free radicals, causing ventilation perfusion mismatch and endothelial injury (42). The endothelial injury causes vasoplegia which leads to haemodynamic instability, resulting in further transfusion of blood products, and increased use of inotropes (45).

The inflammatory response increases capillary permeability resulting in fluid leak into the interstitial space causing pulmonary oedema (41). Studies have shown prolonged postoperative mechanical ventilation (21, 31, 46), acute kidney injury, and infection (31) with increased transfusion of blood products.

1.6 Transfusion triggers in paediatric cardiac surgery

Cardiac surgery is associated with perioperative bleeding which may result in the need to transfuse, more so if the patient is on CPB. The Society of Thoracic Surgeons and the Society of Cardiovascular Anaesthesiologist Blood Conservation Clinical Practice Guidelines recommend RPC transfusion in adult patients on CPB for cardiac surgery when Hb drops below 6 g/dL in stable patients and to maintain Hb above 7 g/dL in patients at risk of end organ ischaemia or injury (9). Transfusion guidelines for paediatric patients could not be identified. The transfusion of blood products in paediatric patients has been noted to be guided by the patient's clinical condition depending on the cardiac lesion, haemodynamic status, laboratory parameters (9), and age (43).

Roseff et al (47) suggested RPC transfusion for cyanotic children less than four months when Hct is below 45%. In children greater than four months RPC is transfused if blood loss exceeds 15% of the patient's blood volume or Hct is less than 40% in patients with severe pulmonary disease. These guidelines are stated "to be representing the opinions of the authors and incorporating evidenced-based data when it exists", so its validity is not conclusive.

Table 1.2 shows CPB Hb transfusion trigger, minimal prime volume and conservation strategies used in a variety of paediatric studies.

Table 1.2 Cardiopulmonary bypass parameters per study

Study	Trigger Hb/ Hct on CPB (g/dl/%)	Minimum prime (ml)	Conservation strategy
Friesen 1993 (48)	Hb 5	450	MUF
Chauhan 2004 (49)	Hct 24	400	
Miyaji 2007 (45)	Hct 20	140	MUF, CS
Wypij 2007 (50)	Hct 20	unknown	Mini CPB, MUF
Durandy 2007 (24)	Hb 8	140	Mini CPB
Szekely 2009 (32)	Hct 20	Not stated	Antif
Shimizu 2011 (51)	Hct 25	400	
Durandy 2010 (30)	Hb 8, Hb 10 cyanotic	100	MUF
Golab 2011 (52)	Hct 28	300	CS
Hasegawa 2014 (23)	Hct 20	Not stated	Mini CPB, Antif, MUF Supplements
Romlin 2014 (53)	Hct 25	350	MUF, Antif
Agarwal 2014 (26)	Hct 30 single ventricle Hct 25 double ventricle	600	CS, UF Antif
Sang Yoon 2015 (54)	Hct 28	115	
Guzzetta 2015 (55)	Hct 30	250	MUF
Lin 2015 (56)	Hb 10 acyanotic Hb 14 cyanotic	Not stated	Antif
Jobes 2015 (57)	Hct 25	300 4.4	MUF

***** Hb-haemoglobin; Hct-haematocrit; MUF-modified ultrafiltration; UF-ultrafiltration; CS-cell saver; Antif-antifibrinolytic

1.6.1 Use of transfusion triggers

Bharadwaj et al (8) and Guzzetta et al (58) supported what The Society of Thoracic Surgeons and the Society of Cardiovascular Anaesthesiologists Blood Conservation Clinical Practice Guidelines stated about Hb not being the sole trigger for RPC transfusion. Other transfusion triggers might be the general condition and physiological signs. The majority of studies reviewed in Table 1.2 (23, 24, 32, 45, 49,

50, 59, 60) maintained Hb between 7 to 8 g/dL in their paediatric cardiac patients on CPB.

A randomised controlled trial in infant heart surgery on CPB by Wypij et al (50) showed unfavourable outcomes in patient with a Hct below 20% as compared to 25% and 30%. The morbidities included a positive fluid balance and impaired psychomotor development index score after a year. On the contrary, no neurodevelopment impairment was observed in older patients (23) and infants (45) with a Hct below 20% presenting for low risk cardiac conditions.

A randomised paediatric ICU study by Cholette et al (61), in 2011, showed that a Hb of 9 g/dL can be tolerated by the cyanotic patient. A study by de Gast-Bakker et al (62), in 2013, demonstrated that in acyanotic patients, a Hb of 8 g/dL was associated with a decreased length of hospital stay. Another randomised intensive care unit study by Lacroix et al (63) showed no difference in nosocomial infection, duration of ventilation, duration of ICU stay, and reactions to RPC transfusion between the restricted Hb group (7 g/dL) when compared to the liberal group (9,5 g/dL). They suggested not employing restrictive Hb strategies in preterm neonates, children with severe hypoxaemia, actively bleeding, and haemodynamically unstable or cyanotic patients.

1.7 Blood conservation strategies

Blood conservation strategies are employed to decrease allogenic blood transfusion and include the use of autologous blood transfusion, antifibrinolytic agents, miniature CPB, modified ultrafiltration, personnel related factors, point of care tests, and cell salvage.

1.7.1 Preoperative autologous donation

Preoperative autologous donation is donation of blood by the patient preoperatively for use intraoperatively to avoid use of homologous blood as this has unwanted adverse effects. It is not feasible in emergency surgery (64) as it requires time to collect enough blood to use intraoperatively. Some studies seem to exclude children who weigh less than five kg and patients undergoing complex cardiac surgery and low Hb (64-67).

The patient presents to hospital a couple of weeks before the planned operation, and weekly 10 ml/kg of blood is collected from the patient, and stored until the operation

day. This practice is labour intense as it requires the cooperation and commitment of the patient, family and health care workers (65, 66).

These patients need to be given iron and/or erythropoietin to help regenerate the donated blood (7, 23, 64, 65, 67). Although erythropoietin is associated with thrombotic and hypertensive events, the only complication noted was an increase in platelet count (66).

Hibino et al (65) showed a decrease in allogeneic blood transfusion in paediatric surgery in the preoperative autologous blood donation group when compared to the control group. A study by Fu et al (68) showed a decrease in blood transfusion requirement in the group which received retrograde autologous prime. The study was conducted in patients between 15 to 20 kg and only 3,4% (2/59) had complex cardiac conditions.

1.7.2 Antifibrinolytics agents

Antifibrinolytic agents are amino acids which impair conversion of plasminogen to plasmin and prevent binding of plasmin to fibrinogen and fibrin so that the clot is not degraded. They impair platelet aggregation by altering its membranes and kallikrein-kinin system (4).

Aprotinin was the most commonly used antifibrinolytic agent in cardiac surgery until its withdrawal in 2007 due to concerns of increased kidney damage, cardiac failure, thrombosis, and mortality (56). Current practice has moved to the use of tranexamic acid (TXA) or epsilon aminocaproic acid which is 10 times less potent than tranexamic acid. Studies have shown no difference in effectiveness in a comparison between aprotinin and TXA (69, 70), and between TXA and epsilon aminocaproic acid (49) in decreasing blood loss, although there are potency differences between the agents. A decrease in RPC transfusion in patients with congenital heart disease has been demonstrated with the use of antifibrinolytic agents (23, 49, 69-71). No difference was seen in the transfusion of FFP and platelets with the administration of antifibrinolytic agents, and the reason for this was not investigated (71).

The use of antifibrinolytic agents showed a decrease in morbidity when bloodless surgery was achieved(23), probably due to the avoidance of immunomodulation associated with blood product transfusion. These agents can be used for cyanotic and acyanotic cardiac surgery with similar outcomes (51). The effective dose of antifibrinolytic agents on CPB is unknown, but it is recommended to give an initial

bolus dose of TXA is 20 mg/kg intravenously followed by an infusion at 10 mg/kg/h (8). Different institutions have different dosing protocols as noted in the following studies: Machovec et al (72) used TXA 75 mg/kg bolus then an infusion of 75 mg/kg/h on pump; Hasegawa et al (23) used TXA 100 mg bolus then an infusion at 10 mg/kg/h; Giordano et al (71) TXA 20 mg/kg at induction and repeated post CPB; and Chauhan et al (49) administered aminocaproic acid 100 mg/kg or TXA 10 mg/kg three times during the operation.

1.7.3 Miniature CPB

Miniature CPB utilises vacuum assisted venous drainage instead of gravity assisted drainage (59). Small sized oxygenators with integrated arterial filters, short circuits are used, and certain components are omitted to minimise the extent of haemodilution (73). A retrospective audit by Golab et al (74) assessing CPB circuit size between 1997 and 2008, showed that decreasing the CPB circuit size resulted in decreased blood transfusion. Studies have been conducted demonstrating a decrease in blood transfusion with the use of miniature CPB in both paediatric (24, 54) and adult patients (73, 75).

Miyaji et al (45) conducted a retrospective cohort study on infants undergoing cardiac surgery which showed that minimising CPB circuit volume to 140 ml resulted in 64% of patients not receiving blood transfusion. Miniature CPB has made it possible to conduct bloodless cardiac surgery in paediatric patients.

1.7.4 Cell salvage

Cell salvaging is a process involving the collection of blood, mixing it with an anticoagulant, washing and centrifuging it, and finally reinfusing it back to the patient (76-78). The indications for use of the cell saver are: expectations of bleeding of more than 20% of the blood volume (77, 78); multiple antibodies or a rare blood types; and refusal of allogeneic blood transfusion (78). It has been used successfully in patients weighing less than 10 kg (79).

The use of a cell saver has resulted in reduced exposure to allogeneic RPC transfusion (80). There is better oxygen carrying capacity and tissue oxygenation due to the maintainance of 2, 3 diphosphoglycerate concentrations in the salvaged blood (77, 78). The problem with cell salvaging is the shear stress caused by suctioning which results in haemolysis. This can be reduced by applying low suction pressures. Cell salvaging can lead to coagulopathy due to off of washing of platelets, and

clotting factors (78). The safe time duration for storage of salvaged blood to avoid contamination is unknown (78, 80).

1.7.5 Modified ultrafiltration

Modified ultrafiltration is a process of removing residual fluid from the CPB circuit resulting in conservation of red blood cells, plasma proteins and platelets during CPB discontinuation (48). The blood collected by modified ultrafiltration has concentrated Hb, platelets, albumin, and clotting factors (81). This technique has proven to be effective in reducing inflammatory mediators (43, 82) improving pulmonary function (82) and total body fluid volume postoperatively (83).

A prospective study in children by Friesen et al (48) showed a decrease in blood transfusion postoperatively with the use of modified ultrafiltration, and similar findings were observed in a prospective control trial in adults by Gunaydin et al (81).

1.7.6 Personnel related factors

Prolonged operation time in complex procedures increases the risk of bleeding. Kiran et al (77) advices that senior surgeons operate complex cases to attain “bloodless surgery”. The maintenance of haemostasis by surgeons intraoperatively and short operation time reduces the amount of blood lost (84).

1.8 Point of care tests

Thromboelastography is one of the tests used to assess the coagulation status of whole blood under low shear stress. It requires 0.36 ml of blood poured into a cup with a suspended rotating pin. The pin rotates and the degree of rotation is affected by the elasticity and clot strength produced. These changes are transmitted via a torsion wire to a transducer within the machine which eventually displays results as a graph. This is a relatively quick bedside test requiring minimal blood as a sample from the patient as compared to a standard clotting test which must be done in the laboratory (85).

Although small sized, a prospective study by Wagner et al (86) suggests using rotational thromboelastometry to access bleeding tendencies in cardiac surgery. A retrospective randomised control study by Kane et al (25) demonstrated a significant reduction in platelet and cryoprecipitate transfusion during paediatric congenital surgery using a thromboelastogram device. This resulted in guided transfusion of blood products. The study explains the lack of impact of the thromboelastogram on RPC and FFP transfusion when these products are used to prime the CPB circuit.

An activated clotting time is displayed once heparinised whole blood is processed. In comparison, the haemostasis management system gives the heparin dose response curve, activated clotting time, heparin concentration, and protamine dose needed to reverse the heparin (87) . The haemostasis management systems is a better bedside test to assess coagulopathy than activated clotting time as it gives more information than just a single value (88). A cohort study by Machovec et al (89) showed a decreased transfusion exposure with the use of the haemostasis management system compared to activated clotting time. The disadvantage of using activated clotting test in infants is that it is prolonged by antithrombin deficiency, hypothermia and haemodilution (11, 88).

1.9 Benefits of conservation strategies

Bloodless surgery can be achievable as evidenced by the studies in Table 1.3. Paediatric Jehovah's Witness patients have had bloodless corrective cardiac surgery on CPB with good outcomes. Bloodless surgery was possible in 29% (76/259) of patients in a study by Durandy et al (24) as a result of utilisation of blood conservation strategies.

Table 1.3 Bloodless surgeries with associated strategies

Study	Procedure	Prime/Min Hb	Strategy
Carmichael et al (52)	Variable	500 ml Hb 5.5 g/dL	None
Hubler et al (90)	TAPVD repair	190 ml Hb 8 g/dL	Aprotinin CS, miniature CPB
Hasegawa et al (23)	ASD, VSD repair	450 ml Hct 20%	Supplement, erythropoietin, TXA, UF, miniature CPB, ABD, CS
Ratliff et al (91)	Ventricle to aorta tunnel repair, AVR	176 ml Hb 6.1 g/dL	Miniature CPB, UF, CS, TXA, ABD
Boettcher et al (92)	AVSD, TGV	43 ml Hb 10 g/dl	Miniature CPB

*TAPVD-total anomalous pulmonary venous disease; VSD-ventricular septal defect; ASD-atrial septal defect; AVR-aortic valve replacement; AVSD-atrioventricular septal defect; TGV-transposition of great vessels; MUF-modified ultrafiltration, CS-cell saver; ABD-autologous blood donation; Hct-haematocrit ; Hb-haemoglobin; CPB-cardiopulmonary bypass

1.10 Cost implications of blood transfusions

Blood products are expensive and use in paediatric cardiac surgery is an almost unavoidable practice. According to the SANBS price list, more processing which is

necessary in the production paediatric patients bold products lead to more expense (93).

There is an increase in the number of blood products transfused compared to the number of donors presenting for blood pooling (9) which shows the scarceness of blood products. A study conducted in Saudi Arabia revealed that a lack of blood products was one of the reasons for cardiac surgery cancelation (94).

Szekely et al (32) showed an association between the amount of blood product transfusions and risk of death, dialysis, low output syndrome, pulmonary failure and infection. An increase in morbidity results in prolonged hospital stay, increasing the cost of patient management (32).

1.11 A review on blood utilisation practices in paediatric cardiac surgery

Jobes et al (57) conducted a 15 year retrospective cohort study on children less than two years of age which showed a decrease in transfusion requirements if fresh whole blood was given. Information about issued blood product units by blood bank was analysed, and the blood product units were considered transfused if they were not returned back to blood bank within a certain period. This study reported the following means (SD) for transfused blood product units: whole blood 1.5 (0.6); RPC 1.3 (1.3); FFP 0.1 (0.4); platelets 0.3 (0.6); and cryoprecipitate 0.2 (0.6).

Keung et al (95), in a retrospective audit of hospital transfusion of RPC units showed that 41,4% of units where transfused in the perioperative period, and of these 49,2% were given intraoperatively. They found that in cardiac surgery, 1663 units of blood were transfused and most transfusions in CPB cases were intraoperatively (74,3%) and in off CPB cases, preoperatively and postoperatively.

A cohort study conducted by Whitney et al (96), in 2013, showed a decrease in transfusion of RPC and cryoprecipitate post CPB following implementation of an algorithm in children less than six months old. Iyengar et al (46) used mainly RPC and FFP intraoperatively and a few patients received platelet and cryoprecipitate.

In Germany, cardiac surgery was found to be second to the Haematology/Oncology department in increased blood utilisation, and this led to the implementation of a blood management program to monitor blood usage in cardiac surgery throughout the patients stay in hospital. The program was aimed to check if blood products are

transfused appropriately by following guidelines at the institution in order to decrease cost and morbidities related to transfusion. (97)

In an audit by Keung et al (95) in patients at the Royal Children's Hospital in Melbourne, an increased perioperative RPC (2359 units) (41%) usage in cardiac surgery, particularly intraoperatively on CPB, was shown. Though the audit by Wade et al (98), in paediatric patients, was not on cardiac patients, it showed that by having set transfusion protocols it is possible to assess if blood products were given appropriately.

1.12 Conclusion

There are multiple factors that increase the risk of blood product transfusion during paediatric cardiac surgery on CPB. It is essential to understand and optimise the physiological status of the patient prior to surgery, and to comprehend the effects that CPB has on blood product transfusion. Proper blood product transfusion planning in conjunction with point of care coagulation testing is necessary for the reduction of blood product transfusion.

1.13 Reference

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SECTION 3

Draft Article

Audit of blood product transfusion in paediatric congenital heart surgery on cardiopulmonary bypass

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Key words: blood transfusion strategies, paediatric congenital cardiac surgery, cardiopulmonary bypass

Abstract

Background

Cardiac surgery is associated with perioperative bleeding which may result in the need for blood transfusion, particularly in paediatric congenital cardiac surgery on cardiopulmonary bypass (CPB). There is a need for regular auditing in order to improve practices.

Methods

Retrospective, contextual, descriptive data of 105 patients were collected for the period January to December 2014.

Results

The median age of patients was 4 (1–6) years, weight 13 (8.4–20) kg, with mean lowest CPB haemoglobin of 8.3 (1.5) g/dL. There was a statistically significant difference in median red packed cells (RPC), platelets and cryoprecipitate units per patient transfused across four Risk Adjusted classification for Congenital Heart Surgery categories ($p=0.03$, $p=0.0013$, $p=0.0001$ respectively). There was statistically significant correlation between transfused fresh frozen plasma units with CPB time ($r=0.2634$, $p=0.0199$) and RPC units ($r=-0.4654$, $p<0.001$).

Conclusion

Although no standardised transfusion guidelines were available, overall blood product transfusion was comparable to reported practices.

Introduction

Blood products are a scarce commodity in South Africa, as reported by the South African National Blood Service. [1] Cancellation of surgical cases has been reported due to depletion of blood products from the blood blank. [2] Blood products are transfused commonly in paediatric cardiac surgery on cardiopulmonary bypass (CPB). [3] Blood product transfusion is intended to treat anaemia, improve oxygen-carrying capacity and oxygen delivery to tissues, and to maintain haemostasis. [4]

Transfusion of blood products is not without complications, and can result in haemolytic and non-haemolytic adverse reactions. [5] In paediatric cardiac surgery on CPB, blood product transfusion has been associated with cardiovascular instability, acute kidney injury, [6] delayed extubation time,[7] prolonged mechanical ventilation, infection, [6, 8, 9] and increased risk of postoperative bleeding. [10]

The World Health Organisation (WHO) recommends the provision of disease-free blood products, and the promotion of appropriate usage of blood products by health care providers. [11] The implementation of blood conservation strategies to reduce blood product transfusion in paediatric cardiac surgery is recognised by the WHO. [12] These strategies have made it possible to perform bloodless paediatric cardiac surgery on CPB, [13] and have also been used successfully in Jehovah's Witness patients. [14, 15]

Blood transfusion guidelines are available for adult cardiac surgery patients, [16] but could not be found for paediatric patients. The lack of standardised guidelines in paediatrics cardiac surgery could be because of multiple factors that influence blood product transfusion in this patient population. [6] There are still controversies regarding the safest haemoglobin on CPB in paediatric cardiac surgery. [13, 17-19] A randomised controlled trial, from the Boston Children's Hospital, revealed a poor psychomotor developmental index after a year in young patients with a range of congenital cardiac conditions with haematocrits below 21.5% on CPB. [17] In contrast, no neurodevelopment impairment was observed in older patients [13] and infants [18] with a haematocrit below 20% presenting for low risk cardiac conditions. There were no outcome differences reported between the liberal (9.5 g/dL) and restrictive (7 g/dL) haemoglobin strategies during the postoperative period in paediatric patients post acyanotic cardiac surgery in one study. [19]

The WHO requires appropriate blood product use by health care providers, which can be assessed by regular audits. Although the appropriateness of blood product transfusion during cardiac surgery is undefined, it is essential to audit institutional practices. Audits are intended to evaluate practices and identify the need to change or modify these practices to improve blood product utilisation. This study aimed at evaluating transfusion practices in paediatric patients at a tertiary hospital as our practice had not been audited previously. The objectives of the study were to primarily describe the demographic and clinical characteristics of the study participants, and secondarily to assess the differences in the transfused blood product units between RACHS categories and patients' weight categories.

Methods

A retrospective, contextual, descriptive study was conducted at Charlotte Maxeke Johannesburg Academic Hospital. Approval to conduct the study was obtained from the Human Research Ethics Committee (Medical) and other relevant authorities. Informed consent was not required as this was a retrospective study. Data were collected by one author (CTB). Patient confidentiality was maintained by assigning numbers to patient data, and raw data was accessed by the author and supervisor.

Data were collected for patients younger than 18 years of age who underwent cardiac surgery on CPB for congenital heart disease during the period between 1 January and 31 December 2014. The charts of the anaesthetists, perfusionists, and the ICU were reviewed for relevant data. Data collected included patient demographics, cardiac lesion and operation, preoperative platelet count, perioperative anticoagulation therapy, perioperative haemoglobin, CPB time, aortic cross-clamp (AOX) time and intraoperative blood products used. Blood products transfused were represented as units of products transfused to the patients as the practice in the department is not that of documenting products by millilitres. The practice also involves transfusion over a period of time of products commenced intraoperatively, into the postoperative period (no longer than four hours for RBCs and 30 minutes after thawing for fresh frozen plasma (FFP)). A unit of RPC has a volume of approximately 300 mls, FFP approximately 225 mls, platelets approximately 160 mls, and cryoprecipitate approximately 15 mls. Patients who were Jehovah's Witness, and patients with missing or illegible data were excluded.

Data collection, management and processing was performed using Microsoft® Excel for Windows, and the analysis was conducted using Stata ®14 (StataCorp.2015,

Stata Statistical Software: Release 14. College Station, TX: StataCorp LP). Descriptive analysis were done using tables of frequencies and percentages, mean (SD) and median (IQR) where appropriate, and were presented according to Risk Adjusted classification for Congenital Heart Surgery (RACHS) categories as this denotes the complexity of the cardiac surgery. [20] The Kruskal-Wallis and One-way Anova analysis of variance were conducted to determine the median or mean differences of clinical variables across RACHS and weight categories. The Dunn's comparison with Holm-Sidak stepwise adjustment was performed as a post-hoc test to the Kruskal-Wallis to find where the statistical significant difference was between the groups with statistical significant differences. A pairwise correlation test was performed to assess the linear relationship between RPC, FFP, and CPB time. A p-value less than 0.05 was considered statistically significant.

Results

A total number of 121 patients were eligible to be included in the study. Of these, 16 patients were excluded due to missing data pertaining to preoperative results (4), anaesthetic charts (2), perfusionist charts (5), and intensive care unit charts (5). There were 6 (5.7%) redo surgery patients who were included in the study as their primary surgery had been undertaken outside of the study period. No patients were included in the study more than once.

The patient demographics are presented in Table 1.1 according to patients' respective RACHS categories. There were no patients in RACHS category 5; therefore, the category is excluded from the tables.

Table 1. 1 Demographics according to RACHS category

Parameter	RACHS 1	RACHS 2	RACHS 3	RACHS 4
Demographics				
Patient n (%)	13 (12.4)	62 (59)	27 (25.7)	3 (2.9)
Male n (%)	5 (9.4)	34 (64.2)	12 (22.6)	2 (3.8)
Female n (%)	8 (15.4)	28 (53.8)	15 (28.8)	1 (1.9)
Age (yr) Median(IQR)	5.5 (3.5 - 6.25)	4 (1 - 6)	4 (1 - 7)	0.08 (0.08 -1.04)
Wt (kg) Median (IQR)	18 (13 - 20)	12 (9 - 19)	13 (8 - 22)	3.4 (3.3 - 3.45)
Congenital heart lesions n (%)				
ECD	11 (25.6)	21 (48.8)	11 (25.6)	0 (0)
GVA	2 (28.6)	0 (0)	2 (28.6)	3 (42.9)
TOF	0 (0)	28 (100)	0 (0)	0 (0)
Valve abnormal	0 (0)	13 (56.5)	10 (43.5)	0 (0)
CC abnormal	0 (0)	0 (0)	4 (100)	0 (0)

*Wt-weight; ECD-endocardial cushion defects; GVA-great vessel anomalies; TOF-Tetralogy of Fallot; CC-cardiac chamber; RACHS-Risk Adjusted classification for Congenital Heart Surgery

The preoperative haemoglobin and platelet count are presented in Table 1.2. There was no significant difference in preoperative platelet count, and preoperative haemoglobin across RACHS categories.

Table 1. 2 Preoperative platelet count and haemoglobin

Parameters Mean (SD)	RACHS 1	RACHS 2	RACHS 3	RACHS 4	p value
Platelets (10^9/L)	317.3 (89.8)	294.8 (128.7)	327 (144.6)	277.7 (96.4)	0.855
Hb (g/dL)	12.7 (1.3)	14.7 (3.7)	14.3 (3.6)	11.1 (2.6)	0.16

*RACHS-Risk Adjusted classification for Congenital Heart Surgery, Hb-haemoglobin

Records showed that aspirin was administered preoperatively in only 3 (2.9%) patients with no doses documented, and these patients where from RACHS category 2. A bolus dose of 300 to 500 IU/kg heparin was given by anaesthetists before initiation of CPB. The perfusionists administered additional heparin during CPB with a mean (SD) dose of 1.8 (1.4) mg/kg.

The type of CPB clear fluid prime for the 105 patients was not clearly stated on the charts. Ten out of 105 (9.5%) patients did not receive clear prime fluid on CPB. The median (IQR) fluid volume used was 800 (500–1000). Albumin was added to the CPB in 32 (30.5%) patients at a mean (SD) dose of 9.7 (4.1) ml/kg.

The median values for AOX and CPB time in minutes between the RACHS categories are shown in Table 1.3. AOX and CPB times were statistically significantly different between RACHS scores. There was a statistically significant relationship between FFP units transfused with CPB time (r=0.2634, p=0.0199), and RPC units (r=-0.4654, p<0.001) transfused.

Table 1. 3 CPB and AOX time in minutes according to RACHS category

Parameter Median (IQR)	RACHS 1	RACHS 2	RACHS 3	RACHS 4	p value
AOX time (min)	18.5 (11- 40.5)	76 (50- 123.5)	89 (57- 120)	157 (112- 193)	0.0002*
CPB time (min)	55 (50- 97.5)	123 (94.5- 89.5)	143 (100- 198)	294 (257- 447)	0.0001*

* p < 0.05; AOX-aortic cross clamp; CPB-cardiopulmonary bypass; RACHS-Risk Adjusted classification for Congenital Heart Surgery

Table 1.4 shows units of blood product transfused according to RACHS categories. Platelets and cryoprecipitate were given solely by anaesthetists. Only 2 (1.9%) patients had a transfusion-free operation and they were from the RACHS category 1.

Table 1. 4 Blood product units transfused according to RACHS category

Products n (%)		RACHS 1	RACHS 2	RACHS 3	RACHS 4	Total
RPC	**Total**	11 (9.9)	66 (59.5)	28 (25.2)	6 (5.4)	111 (100)
	Anaesthetists	0 (0)	8 (7.2)	2 (1.8)	1 (0.9)	11 (9.9)
	Perfusionists	11 (9.9)	58 (52.3)	26 (23.4)	5 (4.5)	100 (90.1)
FFP	**Total**	2 (3.4)	41 (70.7)	15 (25.7)	0 (0)	58 (100)
	Anaesthetists	2 (3.4)	21 (36.2)	12 (20.7)	0 (0)	35 (60.3)
	Perfusionists	0 (0)	20 (34.5)	3 (5.2)	0 (0)	23 (39.7)
Platelets (Anaesthetists)		0 (0)	16 (51.6)	11 (35.5)	4 12.9)	31(100)
Cryoprecipitate (Anaesthetists)		0 (0)	17 (60.7)	6 (21.4)	5 (17.9)	28 (100)

*RPC-red packed cells; FFP-fresh frozen plasma; RACHS-Risk Adjusted classification for Congenital Heart Surgery

A Kruskal Wallis test showed a statistically significant difference between median RPC, cryoprecipitate, and platelet units transfused between RACHS categories (Table 1.5). A post-hoc Dunn's test for the median RPC, cryoprecipitate, and platelet units transfused showed the statistically significant difference to be between RACHS 4 and the other three RACHS categories (1, 2 and 3) (Table 1.6). Additionally, a statistically significant difference was found between RACHS category 3 and 1 for platelet unit transfusion (Table 1.6).

Table 1. 5 Median blood product units per patient transfused by RACHS category

Products Median (IQR)	RACHS 1	RACHS 2	RACHS 3	RACHS 4	Total	p value
RPC	1 (1-1)	1 (1-2)	1 (1-1)	2 (2-2)	1 (1-1)	0.03*
FFP	0 (0-0)	0.5 (0-1)	0 (0-1)	0 (0-0)	0 (0-1)	0.053
Platelets	0 (0-0)	0 (0-1)	0 (0-1)	1 (1-2)	0 (0-1)	0.0013*
Cryoprecipitate	0 (0-0)	0 (0-0)	0 (0-0)	1 (1-3)	0 (0-0)	0.0001*

* p < 0.05; RPC-red packed cells; FFP-fresh frozen plasma; RACHS-Risk Adjusted classification for Congenital Heart Surgery

Table 1. 6 Post-hoc Dunn test of blood product use between RACHS categories

Product	Categories	RACHS 4	RACHS 3	RACHS 2
RPC K Wallis p value = 0.030*	**RACHS 1**	0.009*	0.321	0.302
	RACHS 2	0.018*	0.405	
	RACHS 3	0.022*		
Platelets K Wallis p value = 0.001*	**RACHS 1**	0.001*	0.021*	0.065
	RACHS 2	0.005*	0.123	
	RACHS 3	0.021*		
Cryoprecipitate K Wallis p value = 0.0001*	**RACHS 1**	<0.001*	0.256	0.349
	RACHS 2	<0.001*	0.217	
	RACHS 3	<0.001*		

* p < 0.05; RPC-red packed cells; RACHS-Risk Adjusted classification for Congenital Heart Surgery

Taking into consideration the small sample size in RACHS 4, a further analysis of the RACHS categories into two groups consisting of RACHS 1 and 2, and RACHS 3 and 4, was undertaken and found similar results for platelets and cryoprecipitate (Table 1.7). The significant difference was lost for RPCs.

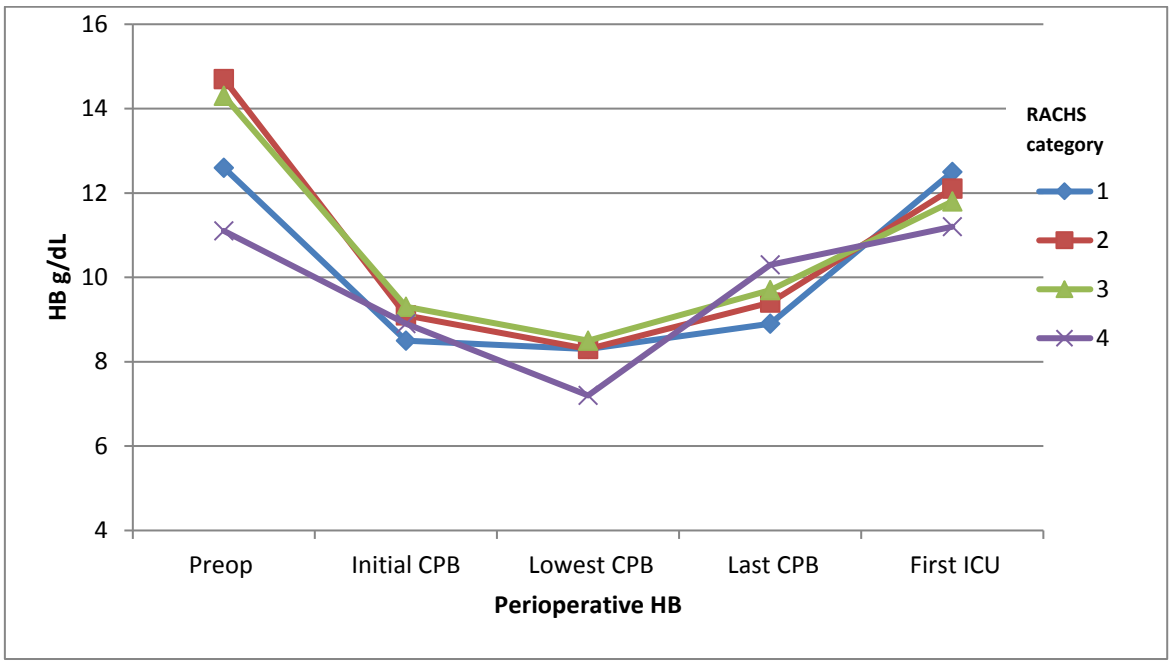
Table 1. 7 Median blood product units per patient transfused between two RACHS category

Products	RACHS 1+2	RACHS 3+4	Total	p value
RPC	1 (1- 1)	1 (1-1)	1 (1-1)	0.4359
FFP	0 (0-1)	0 (0- 1)	0 (0-1)	0.5218
Platelets	0 (0- 0)	0 (0- 1)	0 (0-1)	0.0162*
Cryoprecipitate	0 (0- 0)	0 (0- 0)	0 (0-0)	0.0254*

* p < 0.05; RPC-red packed cells; FFP-fresh frozen plasma; RACHS-Risk Adjusted classification for Congenital Heart Surgery

The mean perioperative haemoglobin levels according to RACHS categories are shown in Figure 1 and Table 1.8. There was no significant difference in mean perioperative haemoglobin levels across the RACHS categories.

Figure 1: Perioperative haemoglobins categorised by RACHS categories



*CPB-cardiopulmonary bypass; ICU-intensive care unit; RACHS-Risk Adjusted classification for Congenital Heart Surgery; preop-preoperative

Table 1. 8 Perioperative haemoglobins across the RACHS categories

Haemoglobin (g/dL)	RACHS 1	RACHS 2	RACHS 3	RACHS 4	p value
Preoperative	12.6 (1.3)	14.7 (3.6)	14.3 (3.6)	11.1 (2.6)	0.16
Initial CPB	8.5 (1.4)	9.1 (1.8)	9.3 (1.5)	8.9 (2.6)	0.61
Lowest CPB	8.3 (1.4)	8.3 (1.6)	8.5 (1.2)	7.2 (1.2)	0.42
Last CPB	8.9 (1.3)	9.4 (1.3)	9.7 (1.2)	10.3 (1.4)	0.33
Initial ICU	12.5 (1.3)	12.1 (2.1)	11.8 (1.9)	11.2 (1.8)	0.72

*CPB-cardiopulmonary bypass; ICU-intensive care unit; RACHS-Risk Adjusted classification for Congenital Heart Surgery

The median blood product units by weight categories are presented in Table 1.9. The RPC, platelets, and cryoprecipitate units transfused were statistically significant across the weight categories. A post-hoc Dunn's test showing where the difference lies between weight categories with regards to cryoprecipitate and RPC unit transfusion shows differences predominantly between weight category >15 kg and other categories, whilst platelet unit transfusion differences were between weight categories < 6 kg and 6 to 15 kg (Table 1.10).

Table 1. 9 Median blood product unit transfusion by weight

Categories Products	Weight <6 kg (n=11)	Weight 6- 15 kg (n=52)	Weight > 15 kg (n=42)	K Wallis p value
RPC	1 (1-2)	1 (1-1)	1 (0-1)	0.001*
FFP	0 (0-0)	0 (0-1)	1 (0-1)	0.087
Platelets	1 (0-1)	0 (0-0)	0 (0-1)	0.038*
Cryoprecipitate	0 (0-1)	0 (0-0)	0 (0-0)	0.009*

* p < 0.05; RPC-red packed cells; FFP-fresh frozen plasma

Table 1. 10 Post-hoc Dunn test of blood product use between weight categories

Products	RPC		Cryoprecipitate		Platelets	
Categories	**<6 kg**	**6-15 kg**	**<6 kg**	**6-15 kg**	**<6 kg**	**6-15 kg**
6-15 kg	0.096		0.049*		0.019*	
>15 kg	0.002*	0.002*	0.004*	0.043*	0.099	0.097

* p < 0.05; RPC-red packed cells

The blood conservation strategies employed were the use of tranexamic acid, cell salvage, and ultrafiltration. A single-blood conservation strategy was used in 36 (34.3%) patients, and two strategies in 45 (42.9%) patients. All three strategies were used in 16 (15.2%) patients, whilst 8 (7.6%) patients had no blood conservation strategy used.

Discussion

The current study was very difficult to analyse because of multiple variables which influence perioperative blood product usage, of which some were not assessed. Guidelines to audit whether blood products were appropriately transfused in paediatric cardiac surgery were not identified. It was also difficult to compare results with literature because of the vast variety within the patient population.

Documentation of blood product amounts transfused by both the anaesthetists and perfusionists were in units and not in millilitres similar to data in a study by Jobes *et al*. [21]

In the current study, patients were categorised according to the RACHS category as it signifies the complexity of the congenital cardiac lesion and surgery. [20] There was an increase in the progression of blood product transfusion across the RACHS categories. Patients in RACHS category 4 had a higher transfusion rate for RPC, platelets, and cryoprecipitate than other groups. These patients were younger and had prolonged CPB and AOX time.

Studies by Kipps *et al.* [9] and Szekely *et al*. [6] also demonstrated that the above factors are associated with increased transfusion of blood products. No FFP was transfused in the RACH category 4 patients with preference shown for cryoprecipitate, which contains concentrated clotting factors in a small volume. [5] This allowed for haemostasis to be achieved without the complication of fluid overload in the patients.

Bloodless paediatric cardiac surgery has been performed successfully with the use of miniature circuits. [13, 14, 18, 22] At our institution, miniature CPB circuits were not utilised at the time of the audit. Perhaps this was the reason for only 1.9% of cardiac surgical cases having bloodless surgery in the current study. Miniature circuits have also resulted in a decrease in the volume of RPC transfusion without an increase in morbidity or mortality. [23] Studies by Redlin *et al.* [24] and Miyaji *et al*. [18] showed higher rates of bloodless cardiac surgery (48%) on patients below 16 kg of weight, and 64% on patients less than 7 kg of weight. A one-year retrospective study by Durandy *et al*. [25] reported 61% of patients between 6 to 15 kg having undergone bloodless cardiac surgery.

The blood products mostly transfused were RPC and FFP, with perfusionists mainly transfusing RPC and anaesthetists transfusing RPC, FFP, cryoprecipitate and platelets. The reason for this might be that the perfusionists primed the CPB circuit with RPC to prevent haemodilution associated with large-volume CPB circuits. [22] As a result, the haemoglobin levels were not significantly different across the RACHS categories throughout the perioperative period. There was an overall decrease in haemoglobin from preoperative levels on initiation of CPB, and an increase to haemoglobin > 10 g/dL on arrival in ICU. A similar perioperative haemoglobin pattern was seen in the cohort study by Redlin *et al.* [24] in their blood transfusion group. This demonstrates the appropriate use of RPC in maintenance of haemoglobin levels.

The anaesthetists transfused FFP, cryoprecipitate, and platelets at the end of CPB empirically to manage bleeding. Only activated clotting time was used as a point of care test, which did not give information about the state of other coagulation system components. A recent cohort by Machovec *et al*. [26] in infant cardiac surgery showed a decreased transfusion exposure with the use of a haemostasis management system compared to activated clotting time. It has become common practice to use intraoperative point of care tests to assess the coagulation status of patients before

transfusion of blood products, as well as blood management programmes in paediatric cardiac surgery. [23, 27] This practice has resulted in decreased blood product transfusions when used in conjunction with algorithms. [26-29] Testing of fibrinogen and platelet function during rewarming has resulted in decreased cryoprecipitate transfusion post CPB in a cohort by Machovec *et al*. [29]

Although there were no blood usage protocols at our institution, the mean haemoglobin on CPB of 8.3 (1.5) g/dL was attained, which is comparable with haemoglobin trigger levels of 7- 8 g/dL observed in other studies. [24, 25] Even though transfusion triggers are set, transfusion of blood products should be individualised to the clinical condition of the patient. [4, 30]

In this study, an expected statistically significant difference was shown in CPB and AOX time across RACHS categories. There was a statistically significant correlation between FFP units transfused with CPB time, and RPC units transfused. Jenkins *et al.* [20] had concluded that a high RACHS category signifying the complexity of the surgery was associated with long CPB time, which increased the risk of blood product transfusion. A study by Redlin *et al*. [24] revealed a significant association between transfusion and CPB time (OR=1.02 CI=1.01-1.03, p=< 0.0001). Another study by Salvin *et al*. [31] showed that patients with an increased CPB and AOX time were transfused more blood products postoperatively.

In the current study, when secondary analysis was conducted by categorising data according to weight, there was no significant difference with median FFP transfusion between the weight categories. There was a statistically significant difference in RPC, cryoprecipitate and platelets transfusion between the weight groups. Studies have shown that low weight is associated with an increase in blood product transfusion. [9, 32]

There are no protocols on the administration of conservation strategies at our institution, but the majority of patients utilised some form of blood conservation strategy, singly or in combination. The impact of the different strategies on blood product use was not assessed as it was beyond the scope of this study.

Only 2.9% of patients received aspirin in the current study, and the bleeding risk was not assessed because there was no point of care testing. Aspirin has been

associated with increased RPC transfusion in adult cardiac surgery, [30] but had no effect on bleeding and transfusion in paediatric cardiac surgery. [31]

The current study was retrospective, and depended on the availability of records and record-keeping by colleagues. The study did not look at temperature, metabolic state of the patient, or intraoperative bleeding which may have contributed to transfusion. The study also did not differentiate between cyanotic and acyanotic cardiac lesions as data were not clear on this. Further studies should be conducted to demonstrate if there is a relationship between our practice and morbidity and mortality. Transfusion protocols together with the utilisation of point of care test should be considered.

Conclusion

The use of RPC was different between RACHS categories whilst maintaining similar haemoglobin levels despite the absence of set transfusion triggers and miniature circuits. The pattern of haemoglobin maintenance was similar to one study. The transfusion of other blood products was empirical as no point of care tests were utilised. The use of triggers, algorithms, and point of care testing in paediatric cardiac patients may result in a decreased level of blood product transfusion.

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SECTION 4

Appendices

Appendix 1: Human Research Ethics Committee (Medical) approval

Human Research Ethics Committee (Medical)

Research Office Secretariat: Senate House Room SH 10005, 10th floor. Tel +27 (0)11-717-1252
Medical School Secretariat: Medical School Room 10M07, 10th Floor. Tel +27 (0)11-717-2700
Private Bag 3, Wits 2050, www.wits.ac.za. Fax +27 (0)11-717-1265

07 August 2015

To Whom It May Concern

SUBJECT: **CONFIRMATION OF STUDY APPROVAL**

Protocol Ref No: M150710

Protocol Title: Audit of blood product transfusions in paediatric congenital heart surgery on cardiopulmonary bypass.

Principal Investigator: Dr. C T Bayebaye

Department: Anaesthesiology

This letter serves to confirm that the Human Research Ethics Committee (Medical) has approved the above mentioned study. In order for a clearance certificate to be issued, the researcher is required to submit written approval to conduct the study in your district/institution.

Should you have any queries, you may contact me at tel 011 717 2656/1234 or by email langutani.masingi@wits.ac.za.

Yours Faithfully,

.....

Mr Langutani Masingi
Administrative Officer
Human Research Ethics Committee (Medical)

UNIVERSITY OF THE WITWATERSRAND
OFFICE OF THE DEPUTY VICE CHANCELLOR RESEARCH
07 AUG 2015
RESEARCH OFFICE
JOHANNESBURG

Appendix 2: Postgraduate approval

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

Private Bag 3 Wits, 2050
Fax: 027117172119
Tel: 02711 7172076

Reference: Ms Thokozile Nhlapo
E-mail: thokozile.nhlapo@wits.ac.za

09 October 2015
Person No: 1029445
PAG

Dr TC Bayebaye
P.O.Box 72
Monato
0331
South Africa

Dear Dr Bayebaye

Master of Medicine: Approval of Title

We have pleasure in advising that your proposal entitled *Audit of blood product transfusion in paediatric congenital heart surgery on cardiopulmonary bypass* has been approved. Please note that any amendments to this title have to be endorsed by the Faculty's higher degrees committee and formally approved.

Yours sincerely

Mrs Sandra Benn
Faculty Registrar
Faculty of Health Sciences

Appendix 3: Data collection spreadsheet

Participant number	1	**2**	**3**	**4**	**5**	**6**
Demographics						
• Age						
• Gender						
• Weight						
• Cardiac lesion						
• Aortic cross clamp time						
• CBP time						
• Resternotomy operations						
Preoperative anticoagulant						
Platelets preoperative						
CPB prime						
• Fluid type						
• Volume (ml)						
• Anticoagulant						
HB						
• Before CPB						
• During CPB						
• After CPB						
Anaesthetist blood product volume (ml)						
• RBC						
• FFP						
• Platelet						
• Cryoprecipitate						
Perfusionist blood product volume (ml)						
• RPC						
• FFP						
• Platelet						
• Cryoprecipitate						
Blood conservation strategies						
• Cell saver						
• Autologous transfusion						
• Miniature CPB						
• Antifibrinolytic agent						
• Ultrafiltration						
• Other						

SECTION 5

Proposal

Audit of blood product transfusion in paediatric congenital heart surgery on cardiopulmonary bypass

Student : Caroline Tumelo Bayebaye

Student number: 1029445

Supervisor: Dr P Motshabi

Department of Anaesthesiology

Introduction

The use of blood products has evolved from transfusion of animal blood to humans and then human blood to humans (1). Blood product transfusion has become a common practice in paediatric cardiac surgery on cardiopulmonary bypass (CPB) (2). This is because of these patients' small body size and blood volume relative to the CPB circuit size (2-7).

Blood products are transfused to treat anaemia, improve oxygen carrying capacity, improve oxygen delivery to tissues, and to maintain haemostasis (8). The most commonly used blood products in cardiac surgery are red packed cells, fresh frozen plasma, platelet, and cryoprecipitate. Although benefits to transfusing blood products exist, this practice is costly and hence the need for blood products to be infused only when there are valid indications. Adverse reactions due to blood product transfusion are a concern as are transfusion transmitted infections although they do not occur commonly (9-11).

The transfusion of blood products in paediatric cardiac surgery on CPB is associated with prolonged mechanical ventilation, infection, (4, 12, 13), cardiovascular instability (4), and acute kidney injury (4, 14). These morbidities may result in the patient staying in the intensive care unit or hospital for prolonged periods thereby increasing the cost of managing a single patient.

There are blood conservation strategies that have been implemented to reduce blood product transfusion during paediatric cardiac surgery. These includes the use of miniature CPB circuits (15, 16) and ultrafiltration (17, 18), which also decreases the inflammatory response associated with CPB (5, 19-21), cell salvaging (17, 22) and preoperative autologous donation (23, 24). The use of antifibrinolytic agents has also shown a decrease in postoperative blood loss (25-27).

One of the objectives of the World Health Organisation is to promote the appropriate use of blood products (28).The Society of Thoracic Surgeons and the Society of Cardiovascular Anaesthesiologists Blood Conservation Clinical Practice Guidelines are guidelines established from adult cardiac patients, and are not clear on the use in the paediatric patient specifically (7). However, there are several studies done in paediatric patients with trigger haemoglobin levels on CPB of 7-8 g/dL for the patient coming for cardiac surgery (5, 6, 20, 29). Though triggers have been set, the general

condition of the patient should also be monitored to guide on the need for transfusing (8, 30, 31) in order to avoid complications due to a low haemoglobin (29).

Wypij et al (29) conducted a randomised control trial of haematrocit strategies during infant cardiac surgery using hypothermic CPB. The group with a mean haematocrit of around 20% had a high fluid balance, high lactate an hour post CPB, low cardiac index in 24 hours, and poor psychomotor development index score after a year as compared to the high haematocrit group (30%). In the same study there were no differences between patient in the low haematocrit (25%) and high haematocrit (35%) (29).

A randomised trial in stable critically ill intensive care unit paediatric patient showed a decreased transfusion rate in the restricted haemoglobin group (7 g/dL) as compared to the liberal group (9,5 g/dL), and there were no difference in outcomes (32). Other prospective, postoperative randomised controlled trials in the paediatric patient showed that restrictive haemoglobin trigger strategies for the cyanotic patient 9 g/dL (33) and the acyanotic 8 g/dL (34) can be tolerated. The acyanotic patients in the restrictive group had a decreased length of hospital stay as compared to the liberal counterpart with a haemoglobin aimed above 10 g/dL (34) .

Decreasing the haemoglobin transfusion trigger can result in a decrease of cost per patient as less blood products are transfused (34). Avoiding transfusion of blood products will reduce the risk of developing transfusion related adverse effects.

Assessing the appropriate use of blood product transfusion is important as it monitors the utilisation practices of an institution. A study by Wade et al (3) on 85 paediatric patients at a tertiary institution showed an inappropriate use of fresh frozen plasma of 58% (18/41 transfusion episodes) and an appropriate overall blood product transfusion of 83% (153/184 transfusion episodes), but there is no study identified assessing appropriateness in the paediatric cardiac patient.

A retrospective audit of anaesthetic and trauma data merged with the blood bank database on red packed cells unit transfusion was done by Keung et al (2) in a children's hospital. This audit showed that in a two-year period 9838 units of red blood cells where issued in the hospital by the blood bank. Fourty-one percent of the total units were transfused perioperatively, and also indicated that cardiac surgery was the department with the largest number of units transfused, 1663 units. This

study shows that blood products are used markedly so in cardiac surgery, hence the need to assess blood product usage in our setting.

Problem statement

Although blood transfusion is associated with many benefits (8), there is an associated increase in morbidity with the transfusion of blood products in paediatric cardiac surgery on CPB (4, 12, 13). Blood conservation strategies have been implemented to reduce blood product transfusion in paediatric cardiac surgery. No specific guidelines for transfusion of blood products during cardiac surgery on CPB in this patient population could be identified.

Blood products are an expensive and scarce resource and should therefore be transfused only when absolutely necessary (7). The utilisation of blood products in paediatric cardiac surgery on CPB for congenital cardiac disease at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) has not previously been audited.

Aim

The current study aims is to describe the utilisation of blood products in paediatric patients with congenital cardiac disease presenting for cardiac surgery on CPB at CMJAH.

Objectives

The primary objectives of this study are to:

- describe the preoperative platelet count
- describe the preoperative and intraoperative anticoagulant therapy (drug and dose)
- describe the patient's haemoglobin before, during, and after CPB
- describe the type and volume of fluid administered to prime the CPB machine
- describe the types and number of blood products transfused intraoperatively by the anaesthetist
- describe the type and number of blood product units transfused on CPB by the perfusionist
- describe strategies used to minimise blood transfusion during CPB.

The secondary objectives are:

- to analyse the blood products transfused according to RACHS categories and weight categories
- to describe the association between blood products transfused and CPB and aortic cross-clamp times.

Research assumptions

The definitions that will be used in this study are as follows:

Paediatric patients: will include the neonate, infant and child.

Neonate: is a child from birth until one month.

Infant: child older than one month but less than a year.

Child: older than one year but less than 18 years.

Patient records: in this study will include patient file, anaesthetic, perfusionist, and ICU charts and will be referred to collectively as records.

Demarcation of study field

The current study is conducted in the theatre complex of CMJAH affiliated to the Department of Anaesthesiology at the University of the Witwatersrand. CMJAH is a 1200 bed central hospital. The hospital has 23 theatres of which two are for cardio thoracic surgery. On average 170 paediatric cardiac surgeries are done annually.

Ethical considerations

Approval to conduct the study will be obtained from the Human Research Ethics Committee (Medical) and the Postgraduate Committee of the University of the Witwatersrand. Permission will be requested from the CEO of CMJAH (Appendix A) to conduct the study. Permission will be requested from Head of Paediatric Cardio Thoracic Surgery (Appendix B) to access the perfusionists' records and patient ICU records, and the Head of Anaesthesiology to access the anaesthetic records (Appendix C).

This study is a retrospective study and no consent will be requested from the patients. The study will ensure anonymity by not having the patient's name recorded while collecting data. The list of patients included in the study will be generated, and each patient will be allocated a study number and this will be used on the data

collection sheet. The list of patient name will be kept separate from the data collection sheet. Confidentiality will be maintained as only the researcher and supervisors will have access to the raw data. Data will be kept securely for six years after completion of the study.

The current study will be conducted according to the principles of the Declaration of Helsinki (35) and the South African Guidelines for Good Clinical Practice (36).

Research methodology

Research design

A retrospective, contextual, descriptive research design will be followed in this study.

Retrospective is defined as “a dependent variable identified in the present and an attempt is made to determine the independent variable that occurred in the past” (37). In this study the blood transfusion practices from 2014 will be audited.

A contextual study is focused on a specific group in a specific location (38). This study is contextual as it audits records of paediatric cardiac surgery patients, with congenital cardiac diseases, on CPB at CMJAH.

A descriptive study is one in which “ phenomenon are described, or the relationship between variables is examined; no attempt is made to determine cause-effect relationships.” (37) This is a descriptive study as the blood product usage in paediatric cardiac surgery patients on CPB will be described.

Study population

The study population will consist of records of paediatric patients who underwent cardiac surgery for congenital cardiac disease on CPB at CMJAH.

Study sample

Sample method

In this study a consecutive, convenience sampling method will be utilised.

Consecutive sampling according to Endacott et al (39) is “a version of convenience sampling where every available individual or event within an accessible population is chosen.” They further state that this is “the best choice of non-random sampling”

Convenience sampling is a sampling process which includes subjects in the study by chance, because they happen to be “in the right place at the right time” (38). This study will access records of all children who underwent surgery for congenital cardiac disease on CPB during 2014.

Sample size

The sample size will be realised by the number of paediatric patients who underwent cardiac surgery on CPB for congenital heart disease from 1 January to 31 December 2014.

Inclusion and exclusion criteria

The inclusion criteria for this study will be:

- records of all paediatric patients who underwent cardiac surgery on CPB for congenital heart disease during the study period
- legible records.

The exclusion criteria for this study will be:

- records of Jehovah’s Witness patients
- missing or illegible records.

Collection of data

Once all the relevant permissions have been granted the researcher will review the records and exclude those that do not meet the eligibility criteria. The researcher will assign study numbers to all patient records that will be included in the study.

The collected data will be logged onto a Microsoft ® Excel spreadsheet (Appendix D). The following data will be collected:

- demographics (age, gender, weight, type of congenital lesion, CPB time, aortic cross-clamp time, resternotomy operations)
- preoperative anticoagulant therapy
- preoperative platelet count
- perioperative haemoglobin (before CPB, during CPB, after CPB)
- priming CPB machine (type and volume of fluid, anticoagulants)
- type and volume of blood product transfused intraoperatively by anaesthetist
- type and volume of blood product administered by perfusionist

- strategies to minimise blood transfusion (cell saver, miniature CPB, ultrafiltration, autologous blood transfusion, antifibrinolytic agents)
- other.

Data analysis

A biostatistician will assist with the analysis of data using Stata ®14. Data will be analysed using descriptive and inferential statistics. Frequencies and percentages will be used to describe categorical variables, means and standard deviations, or medians and interquartile ranges will be used to describe the continuous variables depending on the distribution of the data. The Kruskal-Wallis or One-way Anova analysis of variance will be conducted to determine the median or mean differences of clinical variables respectively. A p value equivalent to or under 0.05 will be considered significant.

Significance of the study

One of the objectives of the World Health Organisation is to encourage the appropriate utilisation of blood products, hence the introduction of a haemovigilance programme which is also practiced by the South Africa National Blood Service (40). This study will describe whether the transfusion practices at CMJAH are comparable with what is practiced in other institutions and if there are any blood conservation strategies used.

The results from this study will draw attention to the blood transfusion practices in paediatric cardiac surgery patients on CPB at CMJAH and will indicate if a change of practice is necessary to ensure improved use of blood products. The results may further contribute to the development of transfusion protocols for this group of patients in the future.

Validity and reliability of the study

Research should always have validity and reliability and these should be considered while formulating the study design. “Validity indicates whether the conclusions of the study are justified based on the design and interpretation” and it also “refers to the degree to which a measurement represents a true value.” “Reliability represents the consistency of the measure achieved” (41).

- The validity and reliability of this study will be ensured by:

- using an applicable study design
- data being collected by one researcher
- recording data on a standardised spreadsheet
- checking every 10th data entry point
- analysis of data being done in conjunction with a biostatistician.

Potential limitations of the study

The current study depends on data collected from records completed by anaesthetists and perfusionists. Records may be missing, incomplete or illegible resulting in patient exclusion from the study.

This study will be done contextually at CMJAH and the findings may not be generalised to other paediatric patients with congenital heart disease undergoing cardiac surgery on CPB.

Project outline

Month	May-June 2015	July 2015	Aug. - Oct. 2015	Nov.-Dec. 2015	Jan. 2016	Feb.-Mar. 2016	April 2016	May 2016
Literature review and proposal	**X**							
Proposal submission	**X**	**X**						
Permission granted			**X**					
Data collection				**X**	**X**			
Data analysis						**X**		
Article							**X**	
Submit								**X**

Financial plan

The Department of Anaesthesiology will bear the cost of printing and paper.

Description	Price per item	Amount of items	Total
Printing	R1 per page	800	R800
Ring binding for examination submission	R50	2	R100
Binding of final research report	R200	2	R400
Total			R1300

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Appendices

Appendices A: Letter to CEO of CMJAH

858 Quail street

Helderkruin, 1726

24 June 2016

CEO CMJAH

Private Bag X39, Parktown

Johannesburg,2193

RE: Permission to conduct an audit of blood product transfusion practices on paediatric patients who underwent cardiac surgery on CPB.

Dear Sir/Madam

I am Caroline Tumelo Bayebaye a registrar in the Department of Anaesthesiology (WITS) currently doing my MMed research. I hereby request permission to conduct my study which is a retrospective audit of blood transfusion practices on paediatric patients who underwent congenital cardiac surgery in the year 2014 at CMJAH.

Anonymity and confidentiality will be maintained in the study and there will be no cost to the hospital.

The study has been approved by the Postgraduate Committee and the Human Research Ethics Committee (Medical). Please find these approvals attached.

Regards

Dr CT Bayebaye

tumzaa@hotmail.com

0723271758

Appendix B: Letter to Head of Paediatric Cardiothoracic Surgery

858 Quail street

Helderkruin, 1726

24 June 2015

Private Bag X39, Parktown

Johannesburg, 2193

RE: Permission to access perfusionists' and ICU records

Dear Dr Cathy Van der Donck

My name is Caroline Tumelo Bayebaye registrar in the Department of Anaesthesiology (WITS) currently doing my MMed research. My MMed is a retrospective audit of blood product transfusion practices on the paediatric patients who underwent congenital heart surgery on cardiopulmonary bypass from 01 January 2014 to 31 December 2014.

The aim of the study is to describe transfusion practices in the unit and compare them to what is done in other institutions.

I am requesting permission to conduct the study and also to have access to patient ICU and perfusionists' records. The records will be reviewed on the premises and the identity of patients and clinicians will not be included in the study.

The research will be conducted after approval by the Postgraduate Committee and the Human Research Ethics Committee (Medical).

Regards

Dr CT Bayebaye (0723271758)

tumzaa@hotmail.com

Appendix C: Letter to Head of Anaesthesiology at CMJAH

858 Quail street

Helderkruin, 1726

24 June 2014

Head of Anaesthesiology CMJAH

Private Bag X39, Parktown

Johannesburg, 2193

RE: Permission to access anaesthetic charts

Dear Prof Oosthuizen

My name is Caroline Tumelo Bayebaye, a registrar in the Department of Anaesthesiology (WITS). I am currently busy with my MMed research which is an audit of blood product transfusion in paediatric patients who underwent congenital heart disease surgery on bypass from 01 January to 31 December 2014.

I am requesting permission to be able to access the anaesthetic charts to proceed with my study. Patient and clinician identity will not be included in the study and the charts will be reviewed on the premises.

The research will be conducted after approval by the Postgraduate Committee and the Human Research Ethics Committee (Medical).

Regards

CT Bayebaye

tumzaa@hotmail.com

0723271758

Appendix D: Example of data to be collected on spreadsheet

Participant number	1	**2**	**3**	**4**	**5**	**6**
Demographics						
Age						
Gender						
Weight						
Cardiac lesion						
Aortic cross clamp time						
CBP time						
Resternotomy operations						
Preoperative anticoagulant						
Platelets preoperative						
CPB prime						
Fluid type						
Volume (ml)						
Anticoagulant						
HB						
Before CPB						
During CPB						
After CPB						
Anaesthetist blood product volume (ml)						
RBC						
FFP						
Platelet						
Cryoprecipitate						
Perfusionist blood product volume (ml)						
RPC						
FFP						
Platelet						
Cryoprecipitate						
Blood conservation strategies						
Cell saver						
Autologous transfusion						
Miniature CPB						
Antifibrinolytic agent						
Ultrafiltration						
Other						